## EDITORIALS



## Prevention of Psychiatric Problems among Military Personnel and Their Spouses

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It is always important to capture information generated from clinical databases to advance theory and practice. This is certainly the case with two articles in this issue of the *Journal*. One article addresses the secondary prevention of post-traumatic stress disorder (PTSD) by the administration of morphine during resuscitation and early trauma care in U.S. Navy and Marine Corps personnel injured in combat.<sup>1</sup> The other article describes increased mental health problems among wives of deployed U.S. Army personnel.<sup>2</sup>

The search for a "morning-after pill" after exposure to traumatic stress is obviously of great importance. It would be valuable if it could be established that certain pharmacologic interventions, administered shortly after exposure to traumatic stress, could prevent or reduce the likelihood of the development of PTSD later on. In this issue of the Journal, Holbrook and colleagues<sup>1</sup> report that the use of morphine among injured Navy and Marine Corps personnel during early (usually <1 hour) resuscitation and trauma care was significantly and protectively associated with a lower risk of PTSD. This finding adds to a small but growing body of observational and experimental studies that have reported similar results.3,4 Since physical injury from a traumatic event (especially injury that is associated with severe pain) is a risk factor for the later development of PTSD, such findings suggest a potential for prophylactic use of rapid pain reduction among injured, traumatized persons in both military and civilian acute care settings.

What about persons with minor injuries or no injuries in the aftermath of major trauma who do not need morphine to attenuate physical pain?

It is possible that the routine administration of morphine could protect them from subsequent PTSD, but it is unlikely that this could become acceptable in clinical practice. This disorder is understood to develop from Pavlovian fear conditioning in which the adrenergic activation of the amygdala during the traumatic event facilitates encoding of traumatic memories.<sup>3,5,6</sup> Indeed, microinjections of norepinephrine into the amygdala in rats<sup>7</sup> can enhance fear conditioning, and this response can be blocked by propranolol. Adrenergic activation can also be blocked by morphine operating at mu-opioid receptors located both in the amygdala and the locus ceruleus (which houses most of the brain's adrenergic neurons). Presynaptic inhibitory  $\alpha_2$ -noradrenergic receptors operate synergistically with opiate muopioid receptors and also blunt adrenergic activation in both the amygdala and the locus ceruleus.

In short, the thoughtful observations of Holbrook and associates are consistent with current theories about the adrenergic mediation of fear-conditioned traumatic memories. Clearly, the relative contributions of morphine-induced analgesia versus morphine-induced suppression of adrenergic activity must be understood, and the fact that these two mechanisms are not mutually exclusive must be recognized. These results should motivate researchers to redouble efforts to test adrenergic antagonists such as propranolol and clonidine (an  $\alpha_2$ -adrenergic agonist) in the search for a morning-after pill to prevent the later development of PTSD among persons after major trauma.<sup>5,6</sup>

The study by Mansfield and colleagues<sup>2</sup> has a very different focus: the relationship between the

deployment of military personnel and the mental health of their wives. Using medical-record data for outpatient care received by more than 250,000 wives of Army personnel (69% of whom had been deployed to Iraq, Afghanistan, or both war zones), Mansfield et al. found that the wives of deployed soldiers, as compared with the spouses of soldiers who were not deployed, had more outpatient visits for depressive disorders, anxiety, sleep disorders, and acute stress reaction and adjustment disorders. Furthermore, deployments of more than 11 months were associated with the use of more mental health services than deployments of 1 to 11 months.

These important findings raise many questions and should serve as an impetus for more fine-grained, hypothesis-driven research. Since the investigators did not have the exact dates of deployment of the soldiers, they could not assess the temporal relationship between deployment and a mental health diagnosis. In other words, was the presence or absence of the soldier more likely to be associated with mental health problems in the wife? If the former, one might consider the literature showing a relationship between spousal distress and marital dissatisfaction associated with deployment.8,9 PTSD after exposure to combat in male veterans has been associated with distress and the poor psychological well-being of their wives, domestic anger and violence, marital problems due to the numbing and avoidance symptoms of PTSD, a negative effect on parenting, and developmental and behavioral problems among children.10-12 However, if spousal distress was more likely to occur during the deployment itself, one must wonder about the difficulties of being a single parent, constant worry about the safety of the deployed partner, and ongoing behavioral and maturational problems expressed by children dealing with their own concerns about the absent parent.

The answers to other questions should influence policy and clinical practice for the care of spouses and families of military personnel affected by the emotional cycle of deployment. Is it deployment per se, with all the complications of separation and worry about loved ones, that is contributing to more mental health problems? Is the intensity of soldiers' exposure to combat during deployment the critical factor? Is the deleterious effect of deployment on spouses mediated by the presence of PTSD or some other combat-

related problem such as physical injury, traumatic brain injury, another psychiatric or substance-use disorder, aggressive or violent behavior, problems expressed by children, other factors, or all of the above? These questions need to be answered. Since social support provides the strongest protection against the development of psychiatric disorders, and since the family is the major source of social support, improvement in the mental health of spouses and children should also pay dividends in improving the mental health of troops throughout the deployment cycle.

The authors of both articles have generated provocative findings from administrative data sets with important implications for preventive strategies. The observations by Holbrook and colleagues on preventing subsequent PTSD by the administration of morphine during resuscitation and early trauma care raise theoretical and practical questions that require rigorous follow-up. Establishing the efficacy of adrenergic antagonists or some other medications as effective prophylaxis against the later development of PTSD would have a considerable effect on emergency medicine for military personnel and civilians. The observations by Mansfield and colleagues on the effect of the deployment of military personnel on the mental health of their wives have public health implications. Besides the obvious importance of developing appropriate programs to fortify wellness and resilience among spouses and children, such programs might also be expected to prevent psychiatric morbidity among the troops themselves.

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## Preoperative Biliary Stents in Pancreatic Cancer — Proceed with Caution

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Pancreatic cancer is a common and deadly disease that is diagnosed in more than 40,000 patients annually in the United States, where it is the fourth leading cause of cancer-related death. Cancer of the pancreatic head causes biliary obstruction by encasing the distal bile duct in tumor. The only potentially curative option is surgical resection (pancreaticoduodenectomy, commonly referred to as the Whipple procedure).

As originally conceived, the Whipple procedure was performed as a two-stage operation. The first stage involved biliary bypass to relieve obstructive jaundice, and the second stage was performed weeks to months later to resect the tumor and reconnect the bile duct, pancreas, and stomach with jejunal anastomoses. The relief of jaundice was based on the recognition that cholestasis from biliary obstruction impairs immune responses, blood clotting, and other functions that directly affect intraoperative and perioperative complications and, potentially, survival after resection. Because of the perioperative morbidity and prolonged delay before resection, it was natural that nonoperative approaches to obstructive jaundice were used when they became available. Initially undertaken with percutaneous transhepatic biliary drainage, the procedure evolved into endoscopic placement of an internal biliary prosthesis at the time of endoscopic retrograde cholangiopancreatography (ERCP), though with uncertain benefit.1

Moreover, endoscopic decompression of the biliary tree became definitive palliative therapy for relief of obstructive jaundice after three ran-

domized, prospective studies showed similar survival outcomes, decreased hospitalization time, and less use of resources in patients who were treated with endoscopic stent placement, as compared with palliative surgical biliary bypass.<sup>2</sup> It remains a maxim that 80% of patients with distal biliary obstruction from pancreaticobiliary cancer are not candidates for surgical cure because of locally invasive or metastatic disease.3,4 When endoscopic stent placement was introduced, only a subgroup of patients went on to an attempt at a definitive resection surgery (Whipple procedure). This number has decreased further because of the improved detection of unresectable disease with the use of computed tomography, magnetic resonance cholangiopancreatography, and endoscopic ultrasonography.

Should biliary stents be routinely placed preoperatively in patients with potentially resectable pancreatic cancer and malignant obstructive jaundice? In this issue of the Journal, van der Gaag et al.5 report the results of a randomized, multicenter study that compared surgical outcomes with preoperative ERCP for biliary drainage for 4 to 6 weeks, followed by surgery, with surgery alone within 1 week after diagnosis. Important findings included an initial ERCP procedural failure rate of 25%; after a second ERCP, successful biliary drainage was achieved in 94% of the patients. In 46% of the patients, there were ERCPrelated complications of pancreatitis, perforation, bleeding, and cholangitis - some severe enough to prevent subsequent pancreaticoduodenectomy.

The initial rates of ERCP failure and proce-